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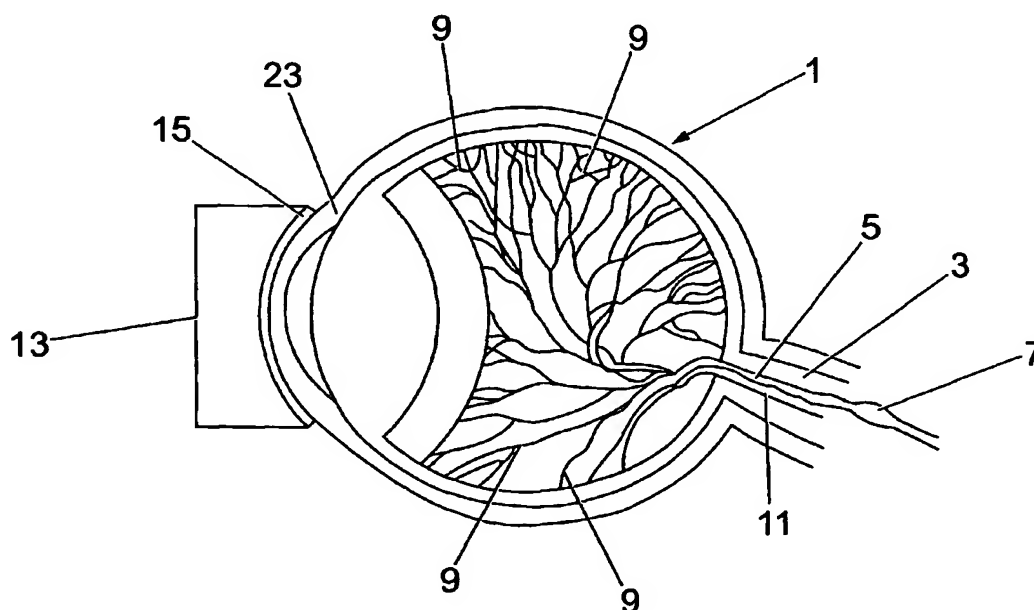
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(54) Title: **VASCULAR IMPEDANCE MEASUREMENT APPARATUS**



(57) Abstract: Apparatus and method for the measurement of vascular impedance of the ocular circulation *in vivo* are provided. A pressure pulse waveform is recorded from measurement of the intraocular pressure, and the velocity profile of blood flow in the retrobulbar circulation is recorded. These two readings are used to calculate the vascular impedance modulus.

1     Vascular Impedance Measurement Apparatus

2

3     The present invention relates to apparatus for  
4     measuring vascular impedance.

5

6     The complications of cardiovascular disease  
7     represent the leading cause of morbid and mortal  
8     events in Western society. At present, diagnostic  
9     procedures are designed to assess the extent and  
10    severity of blood vessel damage when symptoms  
11    present or with the occurrence of vascular events.  
12    The diagnostic challenge is to detect abnormal  
13    structure and function in the vascular system at an  
14    early pre-clinical stage. The ability to detect and  
15    monitor sub-clinical arterial damage has the  
16    potential to refine cardiovascular risk  
17    stratification and enable early intervention to  
18    prevent or attenuate disease progression.

19

20    Traditionally, the arterial circulation has been  
21    considered a steady-flow system characterised by

1 mean arterial pressure that represents the product  
2 of cardiac output and total peripheral resistance.

3  
4 The pulsatile component of pressure is determined by  
5 the pattern of left ventricular ejection and the  
6 stroke volume. The compliance characteristics of the  
7 arterial circulation has been largely ignored in  
8 prior haemodynamic studies.

9  
10 The importance of assessing arterial wall integrity  
11 has been highlighted by studies demonstrating that a  
12 reduction in the pulsatile function or compliance  
13 characteristics of large arteries represents a  
14 powerful independent risk factor for future  
15 cardiovascular events. Accumulating evidence  
16 suggests that abnormalities in the pulsatile  
17 characteristics of arteries occur early in disease  
18 processes associated with increased cardiovascular  
19 risk. Importantly, impaired pulsatile arterial  
20 function is recognised as an independent predictor  
21 of risk for vascular events in patients with various  
22 disease states including coronary heart disease,  
23 congestive heart failure, hypertension and diabetes  
24 mellitus.

25  
26 Studies relating outcome to abnormalities in  
27 pulsatile function have focused on large arteries,  
28 although analysis of arterial pressure pulse  
29 waveforms suggest that the earliest abnormalities in  
30 arterial structure and function resides in the  
31 microcirculation.

32

1 The study of this section of the vasculature has  
2 been hindered by the lack of a non-invasive,  
3 reproducible and repeatable technique capable of  
4 assessing the compliance characteristics or  
5 pulsatile function of small arteries and arterioles.

6  
7 Physiologically, the impedance load or opposition to  
8 flow presented by the circulation is measured  
9 invasively by analysing the altered pressure/flow  
10 relationships and pulse contour parameters produced  
11 through the effects of disease on the structural and  
12 functional components of the arterial system. Input  
13 impedance relates simultaneously recorded pressure  
14 and flow waveforms under specific mathematical  
15 conditions. The haemodynamic properties of the  
16 system can be quantified as the impedance concept  
17 permits the heart and arteries to be considered  
18 separately and their interaction understood as a  
19 function of pump and load properties. As pressure  
20 and flow waves are periodic and continuous, Fourier  
21 series methods can be used to generate the impedance  
22 function. The modulus at each harmonic in the  
23 Fourier series is the ratio of the pressure modulus  
24 to the flow modulus at that harmonic and the phase  
25 at each harmonic is the difference between pressure  
26 phase and flow phase at the same harmonic. As the  
27 impedance of a vascular bed varies with frequency,  
28 complete specification of pulsatile pressure and  
29 flow relationships takes the form of the spectrum of  
30 moduli and phase angles versus frequency<sup>5</sup>.

31

1 Characteristic impedance (the inverse of arterial  
2 compliance) defines the relationship between  
3 pressure and flow in an artery or arterial network  
4 when pressure and flow waves are not influenced by  
5 wave reflections. These conditions do not exist in  
6 the arterial system and the input impedance values  
7 oscillate around the characteristic impedance value  
8 because of wave reflection. Wave reflections are  
9 known to exert their greatest influence on impedance  
10 moduli at low frequencies. For higher frequencies,  
11 the input impedance approaches the characteristic  
12 impedance which has been estimated in prior  
13 haemodynamic studies as the arithmetic mean of input  
14 impedance moduli above 2-4 Hz.

15

16 In the prior art, detailed studies of arterial  
17 pressure and flow are only possible through the use  
18 of invasive techniques. Such techniques cannot be  
19 used to monitor changes in the circulatory system of  
20 a patient over time because of the dangers to health  
21 posed by these techniques.

22

23 In accordance with a first aspect of the present  
24 invention there is provided apparatus for the  
25 measurement of vascular impedance of the ocular  
26 micro circulation *in vivo*, the apparatus comprising  
27 intra-ocular pressure measurement means, from which  
28 a pressure pulse waveform is calculable and blood  
29 velocity profile measurement means for measuring the  
30 linear blood flow velocity in the retrobulbar  
31 circulation, means for calculating a vascular

1 impedance modulus from the pressure pulse waveform  
2 and the linear blood flow velocity.

3

4 Preferably the intra-ocular pressure measurement  
5 means is suitable for measuring the maximum and  
6 minimum pressure values of the pulse profile to  
7 calculate a mean intra-ocular pressure.

8

9 Preferably, the apparatus is suitable for measuring  
10 how the pressure pulse waveform and the linear blood  
11 flow velocity vary over the period of a respiratory  
12 cycle.

13

14 Preferably, the means for calculating the vascular  
15 impedance modulus takes into account the

16

17 Preferably, a solid state transducer is used to  
18 measure intra-ocular pressure.

19

20 Preferably, the solid state transducer operates in  
21 conjunction with a suitable telemetry system to  
22 process the data.

23

24 Optionally, an ocular pneumotonometer is used to  
25 measure intra-ocular pressure.

26

27 Preferably the blood velocity profile measurement  
28 means is an ultrasound device.

29

30 Preferably the ultrasound device is a doppler  
31 ultrasound imager.

32

1 Preferably, the apparatus further comprises motion  
2 picture generation means to produce moving images of  
3 an artery.

4  
5 Preferably, the moving images are capable of being  
6 used to ensure that a user of the apparatus can  
7 accurately identify the location of an artery.

8  
9 Preferably the change in the pulsatile intra-ocular  
10 pressure waveform and the linear blood flow velocity  
11 are measured sequentially.

12  
13 Preferably, the means for calculating the vascular  
14 impedance modulus comprises obtaining the fourier  
15 transform of the intra-ocular pressure pulse  
16 waveform and the linear blood flow velocity and  
17 dividing the transformed values of the pulsatile  
18 change in the intra-ocular pressure pulse by the  
19 transformed retrobulbar blood flow velocity.

20  
21 Preferably the pulsatile change in intra-ocular  
22 pressure has a phase associated therewith.

23  
24 Preferably the intra-ocular blood velocity has a  
25 phase associated therewith.

26  
27 In accordance with a second aspect of the present  
28 invention there is provided a method for the  
29 measurement of vascular impedance of the ocular  
30 micro circulation *in vivo*, the method comprising the  
31 steps of: measuring the intra-ocular pressure pulse  
32 waveform of the ocular network;

1 measuring the linear blood flow velocity in the  
2 retrobulbar circulation; and  
3 calculating a vascular impedance modulus from the  
4 intra ocular pressure pulse waveform and the linear  
5 blood flow velocity waveform.

6  
7 Preferably, the pressure pulse waveform and the  
8 linear blood flow velocity are measured over the  
9 period of a respiratory cycle, and their variation  
10 therewith is measured.

11  
12 Preferably, the variations are used in the  
13 calculation of the vascular impedance modulus.

14  
15 Preferably, the method further comprises the steps  
16 of recording moving images of an artery.

17  
18 Preferably, the moving images are used to accurately  
19 identify the location of an artery.

20  
21 Preferably, the change in the pulsatile intra-ocular  
22 pressure waveform and the linear blood flow velocity  
23 are measured sequentially.

24  
25 Preferably, the step of calculating the vascular  
26 impedance modulus comprises the steps of;  
27 obtaining the fourier transform of the intra-ocular  
28 pressure pulse waveform and the linear blood flow  
29 velocity and dividing the transformed values of the  
30 pulsatile change in the intra-ocular pressure pulse  
31 by the transformed retrobulbar blood flow velocity.

32



1 The invention will now be described by way of  
2 example only with reference to the accompanying  
3 drawings in which:

4  
5 Fig. 1 is a diagram of an eye having means for  
6 measuring the intra-ocular pressure using the  
7 principle of applanation tonometry at the front of  
8 the eye;

9  
10 Fig. 2 is a diagram of an eye having means for  
11 measuring the linear flow velocity by interrogating  
12 the retrobulbar circulation from the front of the  
13 eye;

14  
15 Fig. 3 is a graph of the periodic pressure signal as  
16 measured using the present invention plotted against  
17 time;

18  
19 Fig. 4 is a graph of the periodic velocity signal as  
20 measured using the present invention plotted against  
21 time;

22  
23 Fig. 5 is a graph of impedance modulus plotted  
24 against frequency; and

25  
26 Fig. 6 is a graph of phase plotted against  
27 frequency.

28  
29 Figs. 1 and 2 show a first embodiment of the present  
30 invention. Figs. 1 and 2 are diagrams showing some  
31 features of the human eye 1. These include the  
32 optic nerve 3, the ophthalmic artery 5, a bolus of

1 blood contained in the ophthalmic artery 5  
2 positioned outside the ocular vascular network 9.  
3 The vein 11 is also shown.

4  
5 Fig. 1 also shows the means for measuring the intra-  
6 ocular pressure 13, provided, in this example by a  
7 tonometer system applanated to the cornea 23.

8  
9 Fig. 2 shows means for measuring the linear blood  
10 flow velocity in the retrobulbar circulation 17,  
11 connected to the front of the eye. This is an  
12 ultrasonic device that is placed on the eyelid  
13 19, the eyelid 19 being covered with a gel 21 to  
14 ensure that the ultrasound device is properly  
15 coupled to the eye 1. This device measures the  
16 linear velocity of the bolus of blood 7 in the  
17 ophthalmic artery 5.

18  
19  
20 The tonometer system 13 used can employ continuous  
21 airflow pneumotonometry (for example using an  
22 airflow pneumotonometer as provided by Paradigm  
23 Medical Industries) or can use a solid state  
24 transducer (for example as supplied by Smart Lens  
25 DCT) together with suitable telemetry system to  
26 process the detected data. The arterial function  
27 has been found to have a significant dynamic range  
28 of approximately 0-12 Hz, and thus, the choice of a  
29 pneumatic versus a solid state transducer system  
30 will depend on a suitable dynamic range being  
31 provided by the particular tonometer device used. A  
32 probe 15 is applanated on the cornea 23 to record

1 intraocular pressure. The tonometer device 13  
2 samples at 200 Hz with a resolution of 0.01 mmHg and  
3 the signals are acquired over a 20 second period.  
4 Pulsatile variation of intraocular pressure results  
5 from pressure oscillations generated by cardiac  
6 contraction altering the distending pressure in the  
7 vessel walls. Compliance of an artery, or an entire  
8 arterial bed, describes the ability to store a  
9 varying amount of blood. Changes in volume within  
10 the ocular vascular bed will produce an equal change  
11 in volume. The pulsatile ocular waveforms are  
12 recorded after administration of oxybuprocaine 0.4%  
13 drops to anaesthetise the cornea.

14  
15 The variation in intra-ocular pressure as a function  
16 of time reflects the introduction of the bolus of  
17 blood 7 into the ocular vascular network 9. The  
18 ocular vascular network 9 expands to accommodate the  
19 additional volume of blood.

20  
21 As the intra-ocular fluids are incompressible, the  
22 intra-ocular pressure response to the volume change  
23 will depend of the viscoelastic properties of the  
24 vessel network and the ocular rigidity. The  
25 mechanical properties and distending pressures will  
26 vary at different sites in the ocular vascular  
27 network 9 and it is the composite effect of these  
28 influences that determine the intra-ocular pressure  
29 waveform morphology. Whilst the rigidity of the  
30 ocular coat can vary between individuals, the half-  
31 life of the collagen and elastin components are  
32 measured in years. Consequently, the characteristics

1 of these boundary structures would not be expected  
2 to change significantly within an individual over a  
3 period of weeks or months. Therefore changes  
4 recorded in the intra-ocular pressure pulse waveform  
5 will be reflective of alteration in the viscoelastic  
6 properties of the ocular microcirculatory bed.

7  
8 The present invention uses the directly recorded  
9 change in intra-ocular pressure in its analysis and  
10 not the generated flow output measurements from the  
11 device that relate pressure change to volume change  
12 within the eye. The pulsatility of the intra-ocular  
13 pressure is dependent on the pulsatile inflow and  
14 distension of the vessels which is related to the  
15 viscoelastic properties of the ocular circulation.  
16 Scleral rigidity may limit the frequency of pressure  
17 fluctuations but does not cause variation in  
18 pressure.

19  
20 In the example shown in Fig. 2, a colour doppler  
21 ultrasound imager 17 is used to examine the blood  
22 velocity waveform in the retrobulbar ocular  
23 circulation. The ultrasound imager may suitably be  
24 a Phillips ATL HDI3500 Ultrasound Machine.

25  
26 The appropriate blood vessels then have to be  
27 located and identified. One way of doing this is to  
28 employ simultaneous B-scan and doppler imaging.  
29 However, there are a number of practical  
30 difficulties that have to be overcome when  
31 performing this. Firstly, the orbit is three  
32 dimensional but viewing is possible only in two

1 dimensions using the ultrasound machine.  
2 Furthermore, the ophthalmic artery is tortuous and  
3 has many branches and so it is difficult to get  
4 clear views and for the operator to know exactly  
5 where he is looking. There are also wide anatomical  
6 variations in the position and branching nature of  
7 the ophthalmic artery between individuals.

8  
9 These problems have been addressed by recording  
10 real-time colour motion pictures when initially  
11 inspecting the artery in a subject. They are then  
12 played back under 'cineloop review' and, in  
13 conjunction with depth measurements, used to  
14 orientated the operator back to the original  
15 recording site. Pre-recorded velocity waveforms  
16 finally verify dimensional and morphological  
17 authenticity of waveforms under view.

18  
19 The beam from the ultrasound imager can be focussed  
20 using an appropriate software algorithm.

21  
22 The sample volume defined by the imager 17 is placed  
23 over a vessel of interest, in this case, the bolus  
24 of blood 7 and the frequency shifts received are  
25 assembled into a spectral waveform. The spectral  
26 waveform represents the cumulative frequency shifts  
27 present and can be displayed as a time-velocity  
28 waveform.

29  
30 In use, alternate measurements of the arterial pulse  
31 waveform and blood velocity profile are taken.

1 The shape of the linear velocity flow waveform,  
2 recorded in the retrobulbar circulation , is  
3 determined by and is critically dependent on changes  
4 in total cross-sectional area of the ocular vascular  
5 network.

6  
7 Like pressure, flow will also vary at different  
8 sites in the ocular vascular network 9 and the  
9 velocity waveform morphology therefore reflects the  
10 status of the entire ocular vascular network 9. In  
11 essence, the flow velocity waveform derived from the  
12 retrobulbar circulation and the intra-ocular  
13 pressure waveform reflect the sum total of the  
14 various calibre and pressure changes throughout the  
15 ocular vascular bed.

16  
17 Measured over time, changes in the linear flow  
18 waveform can provide information on changes in the  
19 ability of the ocular vascular network to expand  
20 during the cardiac cycle. Such information can lead  
21 to early diagnosis and subsequent early treatment of  
22 disease.

23  
24 The present invention uses linear velocity of flow  
25 in calculating the vascular impedance of the  
26 microcirculation as changes in velocity of flow are  
27 determined by changes in the total cross-sectional  
28 area of the ocular vascular network 9. Furthermore,  
29 the use of linear velocity of flow permits  
30 comparisons of impedance moduli derived from  
31 different arteries and in the same artery under

1     varying conditions. This comparison cannot be  
2     validly made using volume flow measurements.

3

4     Previous work to characterise the arterial system  
5     has been based on the relationship between pressure  
6     and flow recorded at the same position in time and  
7     space. Windkessel analysis is used to apply an  
8     electrical circuit analogy of input impedance to fit  
9     components of total compliance and total resistance  
10    to the distal arterial tree. However, this  
11    technique does not provide unique solutions.

12

13    In contrast to previous work, the present invention  
14    provides for the recording of pressure and velocity  
15    waveforms at different positions on the arterial  
16    tree. In the ocular microcirculation, ophthalmic  
17    flow can be considered giving rise to the  
18    intraocular pressure. This means that an analogy  
19    can be drawn with two port analysis of electrical  
20    circuit design, which relates an input signal to an  
21    output signal. The relationship between the  
22    intraocular pressure and the corresponding  
23    ophthalmic velocity waveform can thus be  
24    characterised.

25

26    The waveforms of pressure and velocity have a  
27    certain periodicity according to the heart rate of  
28    the subject being tested. However, the breathing of  
29    the subject also affects the waveforms. Hence, a  
30    measure of compliance can be made that takes into  
31    account the respiratory variations. This overcomes  
32    an assumption made by use of a normal Windkessel

1 analysis, namely that the pressure flow waveform has  
2 an infinite pulse wave velocity. This measure of  
3 compliance that takes the respiratory variations  
4 into account can be known as the apparent  
5 compliance. It can be used in conjunction with the  
6 two port model to characterise the system.

7  
8 Typical examples of intraocular pressure and  
9 velocity profiles (obtained from the ophthalmic  
10 artery) are shown in Figures 3 and 4.

11  
12 Fig. 3 is a graph of pressure plotted with respect  
13 to time. The figure shows the periodicity of the  
14 pressure fluctuation. The cardiac cycle can be  
15 identified from the period of the pressure  
16 fluctuation as being approximately 0.9 s.

17  
18 Fig.4 is a graph of linear blood velocity plotted  
19 with respect to time. The figure shows the  
20 periodicity of linear velocity fluctuation. The  
21 cardiac cycle can be identified from the period of  
22 the linear velocity fluctuation as being  
23 approximately 0.9s.

24  
25 The sites of data acquisition enable the recording  
26 of pressure and linear velocity waveforms that  
27 provide information about the entire ocular vascular  
28 network and not merely single vessel in the network.  
29 Measurements are obtained sequentially using the  
30 tangent method to align pressure and velocity  
31 waveforms. This technique is employed to ensure  
32 effective alignment of waveforms for analysis. The



1 signals may also be gated to an ECG. Other known  
2 methods may also be employed.

3

4 As seen in Figures 3 and 4, the velocity and  
5 pressure signals are periodic and time dependent and  
6 can thus be represented in the frequency domain by  
7 obtaining their Fourier transform:  $P(\omega) = FT[P(t)]$   
8 and  $V(\omega) = FT[V(t)]$  where FT represents Fourier  
9 transformation. In addition, each frequency  
10 component of pressure and velocity will have its own  
11 associated phase ( $\phi_p$  pressure phase,  $\phi_v$  velocity  
12 phase). The frequency dependent impedance modulus  
13 and phase can be determined from:  $Z(\omega) = P(\omega)/V(\omega)$   
14 and  $\phi(\omega) = \phi_p(\omega) - \phi_v(\omega)$ .

15

16 Figures 5 and 6 show typical plots of  $Z(\omega)$  and  $\phi(\omega)$   
17 for a normal subject.

18

19 The flow and first derivative of pressure occur at  
20 similar time points. As pressure and flow are  
21 obtained sequentially the first derivative of the  
22 pressure waveform is aligned to the flow waveform.  
23 A tangent to end diastole and a tangent to the  
24 initial upstroke in pressure wall intersect at the  
25 "foot" of the waveform. This point is aligned with  
26 the same point on the flow waveform.

27

28 An improved alignment can be obtained by synching  
29 the peak velocity detected by the imager 17 to an  
30 ECG device.

31

1     Frequency domain analysis provides information about  
2     steady-state (resistance) and pulsatile function  
3     (characteristic impedance) of the ocular  
4     circulation. In Fig. 5, the steady state resistance  
5     is shown in area A and the characteristic impedance  
6     in area B. These signals are stored in digital form  
7     and the digitised signals are amenable to analysis  
8     in the time domain with the application of  
9     mathematical models to interpret waveshape changes  
10    in relation to the mechanical properties of the  
11    ocular circulatory bed.

12  
13    The present invention is highly advantageous with  
14    respect to the prior art because it provides a non-  
15    invasive method and apparatus for measuring vascular  
16    impedance and in particular, through interrogation  
17    of the wave shape, of the linear velocity profile of  
18    the blood bolus in the retrobulbar circulation.  
19    Previously, invasive techniques had only been  
20    thought capable of providing information on the  
21    linear velocity profile. Such techniques are  
22    expensive and cannot be used to obtain repeat  
23    results over a period of time for the same subject.  
24    The present invention therefore allows a physician  
25    to monitor changes in the microcirculation of the  
26    eye and to extrapolate the data to make clinical  
27    judgements in various disease states associated with  
28    an increase in cardiovascular events.

29  
30    The present invention is applicable in a number of  
31    areas of clinical research. Some examples are given  
32    below.

1  
2 It has been recognised for many years that  
3 characteristic changes in the arterial pressure  
4 pulse contour occur in many disease states and with  
5 physiological and pharmacological interventions.  
6 Alteration in arterial waveform morphology typically  
7 involves a steepening of the diastolic decay and a  
8 diminution in the amplitude and duration of the  
9 oscillatory waveform that distorts the proximal part  
10 of diastole from a pure monoexponential. The  
11 oscillatory diastolic waveform arises from wave  
12 reflection and damped resonance occurring in the  
13 arterial tree with the major sites of reflected  
14 waves originating in smaller arteries and  
15 arterioles. Loss of the oscillatory diastolic  
16 waveform is recognised as an early marker of altered  
17 vessel wall properties that identifies impaired  
18 pulsatile function of arteries as it can be found in  
19 patients at increased cardiovascular risk without  
20 alteration in total peripheral resistance. This has  
21 been demonstrated in patients with diabetes mellitus  
22 and cigarette smokers. Whilst the microvascular  
23 changes associated with diabetes are well  
24 recognised, the structural changes that are commonly  
25 found in the arterioles of smokers and rarely in  
26 non-smokers, are less well appreciated. These  
27 microvascular abnormalities may account for the  
28 common occurrence of microinfarcts found in  
29 association with diabetes and cigarette smoking that  
30 have hitherto gone unrecognised.  
31

1     Analysis of the arterial pressure pulse waveform can  
2     also be useful in identifying the haemodynamic  
3     action of drug therapy not detected by the  
4     traditional measurement of peripheral resistance.

5

6     Improvements and modifications may be incorporated herein  
7     without deviating from the scope of the invention.

1    CLAIMS

2

3    1.    Apparatus for the measurement of vascular  
4    impedance of the ocular micro circulation *in vivo*,  
5    comprising intra-ocular pressure measurement means  
6    from which a pressure pulse waveform is calculable,  
7    blood velocity profile measurement means for  
8    measuring the linear blood flow velocity in the  
9    retrobulbar circulation, and means for calculating a  
10    vascular impedance modulus from the pressure pulse  
11    waveform and the linear blood flow velocity.

12

13    2.    Apparatus as claimed in claim 1, wherein the  
14    intra-ocular pressure measurement means is suitable  
15    for measuring the maximum and minimum pressure  
16    values of the pulse profile to calculate a mean  
17    intra-ocular pressure.

18

19    3.    Apparatus as claimed in claim 1 or claim 2,  
20    suitable for measuring how the pressure pulse  
21    waveform and the linear blood flow velocity vary  
22    over the period of a respiratory cycle.

23

24    4.    Apparatus as claimed in any preceding claim,  
25    wherein a solid state transducer is used to measure  
26    intra-ocular pressure.

27

28    5.    Apparatus as claimed in claim 4, wherein a  
29    suitable solid state transducer operates in  
30    conjunction with a suitable telemetry system to  
31    process the data.

32

1 6. Apparatus as claimed in any of claims 1 to 3,  
2 wherein an ocular pneumotonometer is used to measure  
3 intra-ocular pressure.

4

5 7. Apparatus as claimed in any preceding claim,  
6 wherein the blood velocity profile measurement means  
7 is an ultrasound device.

8

9 8. Apparatus as claimed in claim 7, wherein the  
10 ultrasound device is a doppler ultrasound imager.

11

12 9. Apparatus as claimed in any preceding claim  
13 further comprising motion picture generation means  
14 to produce moving images of an artery.

15

16 10. Apparatus as claimed in claim 9, wherein the  
17 moving images are capable of being used to ensure  
18 that a user of the apparatus can accurately identify  
19 the location of an artery.

20

21 11. Apparatus as claimed in any preceding claim,  
22 wherein the change in the pulsatile intra-ocular  
23 pressure waveform and the linear blood flow velocity  
24 are measured sequentially.

25

26 12. Apparatus as claimed in any preceding claim,  
27 wherein the means for calculating the vascular  
28 impedance modulus comprises means for;

29 obtaining the fourier transform of the intra-  
30 ocular pressure pulse waveform and the linear blood  
31 flow velocity and dividing the transformed values of  
32 the pulsatile change in the intra-ocular pressure

1 pulse by the transformed retrobulbar blood flow  
2 velocity.

3

4 13. Apparatus as claimed in any preceding claim,  
5 wherein the pulsatile change in intra-ocular  
6 pressure has a phase associated therewith.

7

8 14. Apparatus as claimed in any preceding claim,  
9 wherein the intra-ocular blood velocity has a phase  
10 associated therewith.

11

12 15. A method for the measurement of vascular  
13 impedance of the ocular micro circulation in vivo,  
14 comprising the steps of: measuring the intra-ocular  
15 pressure pulse waveform of the ocular network;  
16 measuring the linear blood flow velocity in the  
17 retrobulbar circulation; and  
18 calculating the vascular impedance modulus from the  
19 intra ocular pressure pulse waveform and the linear  
20 blood flow velocity waveform.

21

22 16. A method as claimed in claim 15, wherein the  
23 pressure pulse waveform and the linear blood flow  
24 velocity are measured over the period of a  
25 respiratory cycle, and their variation therewith is  
26 measured.

27

28 17. A method as claimed in claim 16, wherein the  
29 variations are used in the calculation of the  
30 vascular impedance modulus.

31

1 18. A method as claimed in any of claims 15 to 17,  
2 further comprising the steps of recording moving  
3 images of an artery.

4

5 19. A method as claimed in claim 18, wherein the  
6 moving images are used to accurately identify the  
7 location of an artery.

8

9 20. A method as claimed in any of claims 15 to 19,  
10 wherein the change in the pulsatile intra-ocular  
11 pressure waveform and the linear blood flow velocity  
12 are measured sequentially.

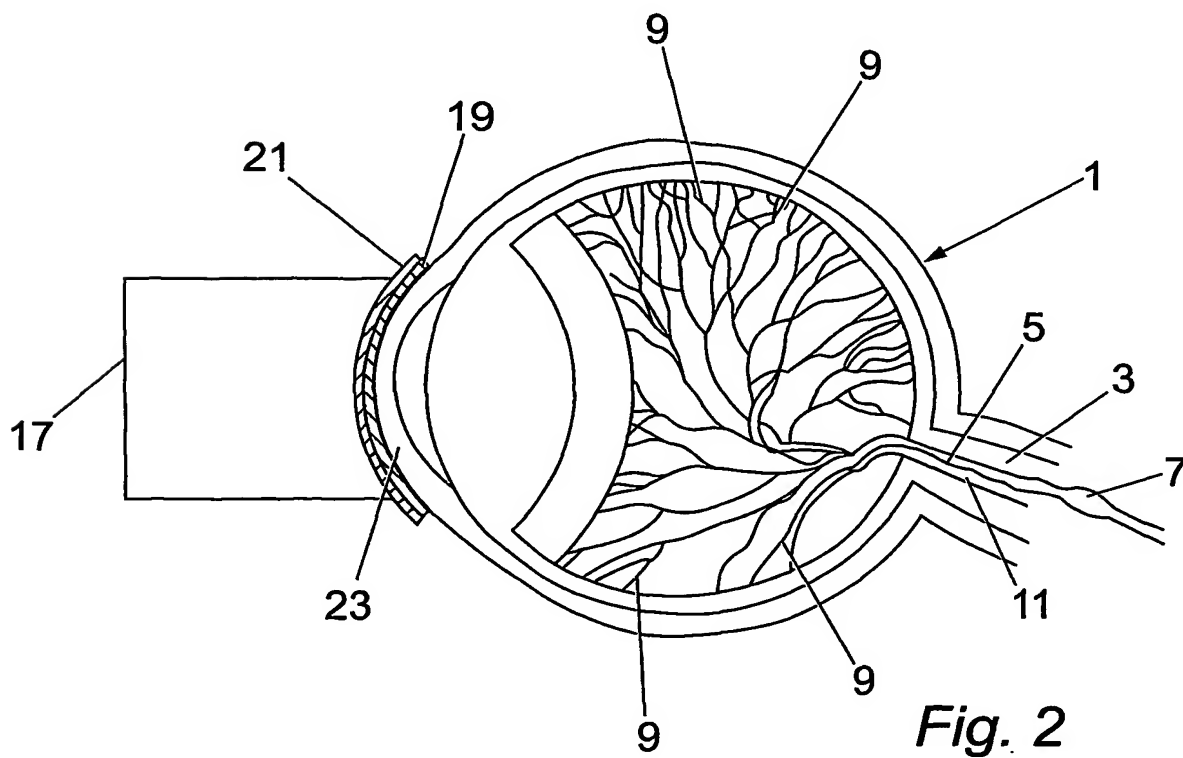
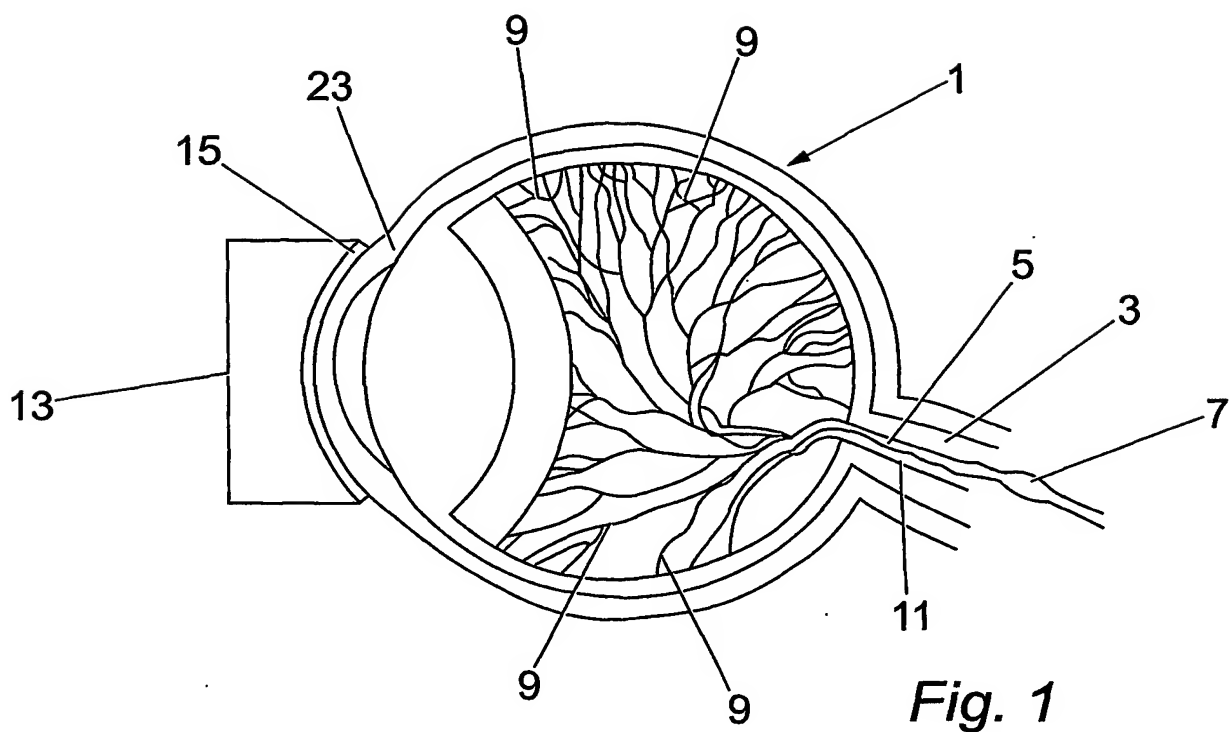
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14 21. A method as claimed in any of claims 15 to 20,  
15 wherein the step of calculating the vascular  
16 impedance modulus comprises the steps of;  
17 obtaining the fourier transform of the intra-ocular  
18 pressure pulse waveform and the linear blood flow  
19 velocity and dividing the transformed values of the  
20 pulsatile change in the intra-ocular pressure pulse  
21 by the transformed retrobulbar blood flow velocity.

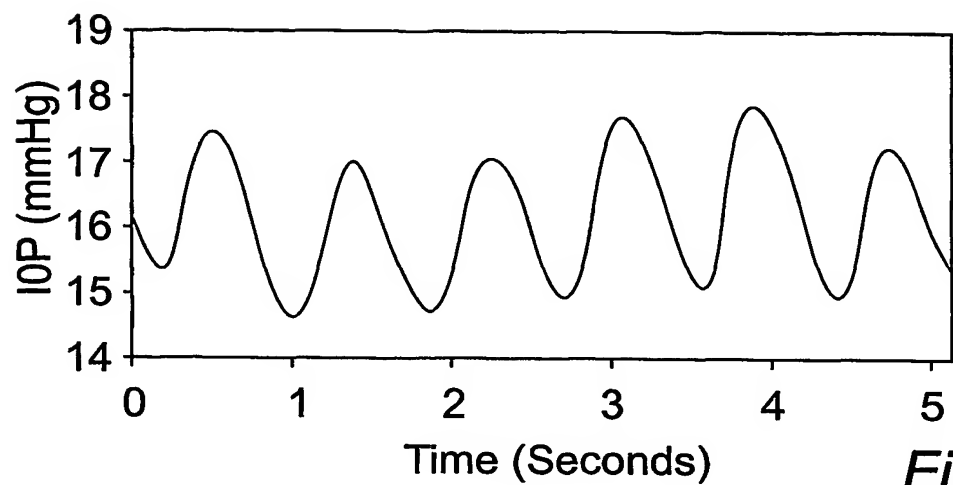
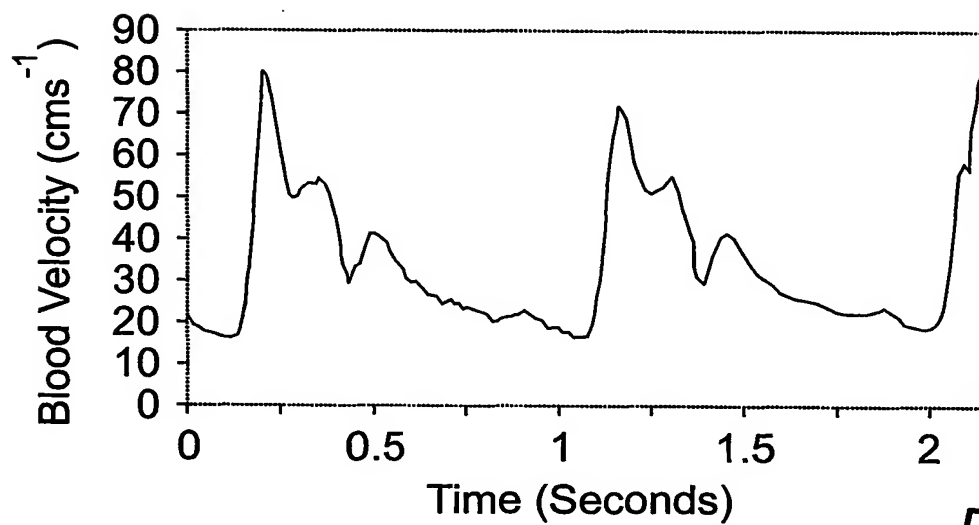
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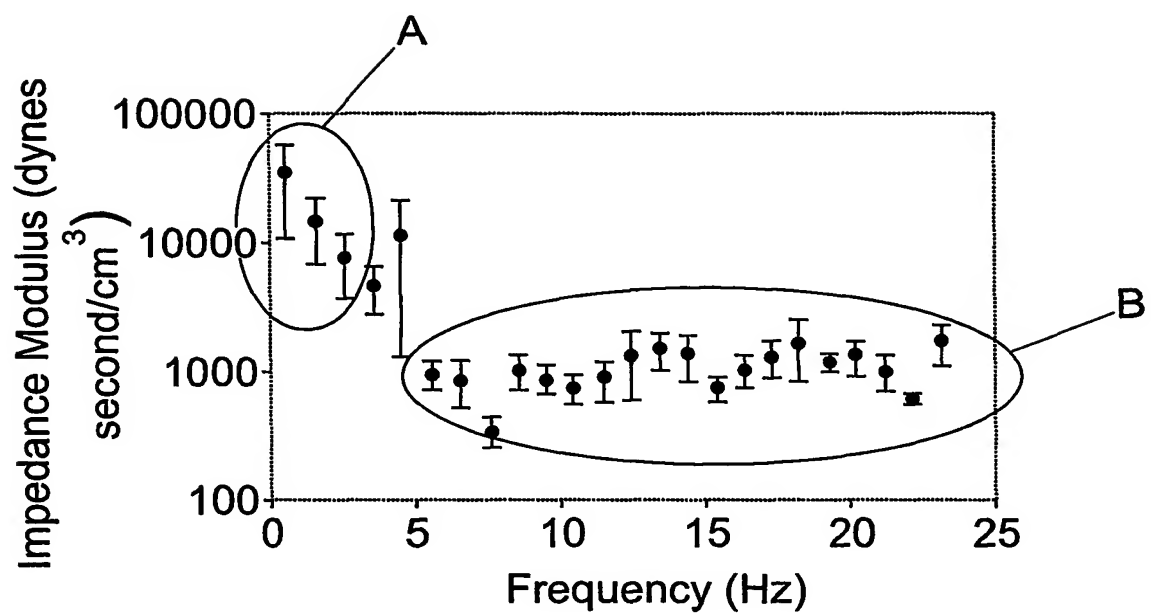
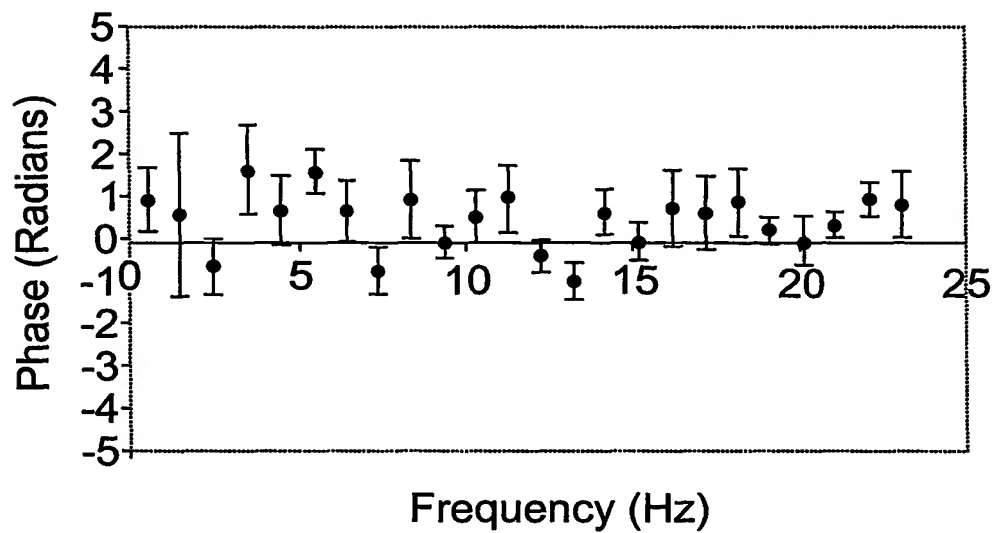
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*Fig. 3**Fig. 4*

3 / 3

*Fig. 5**Fig. 6*

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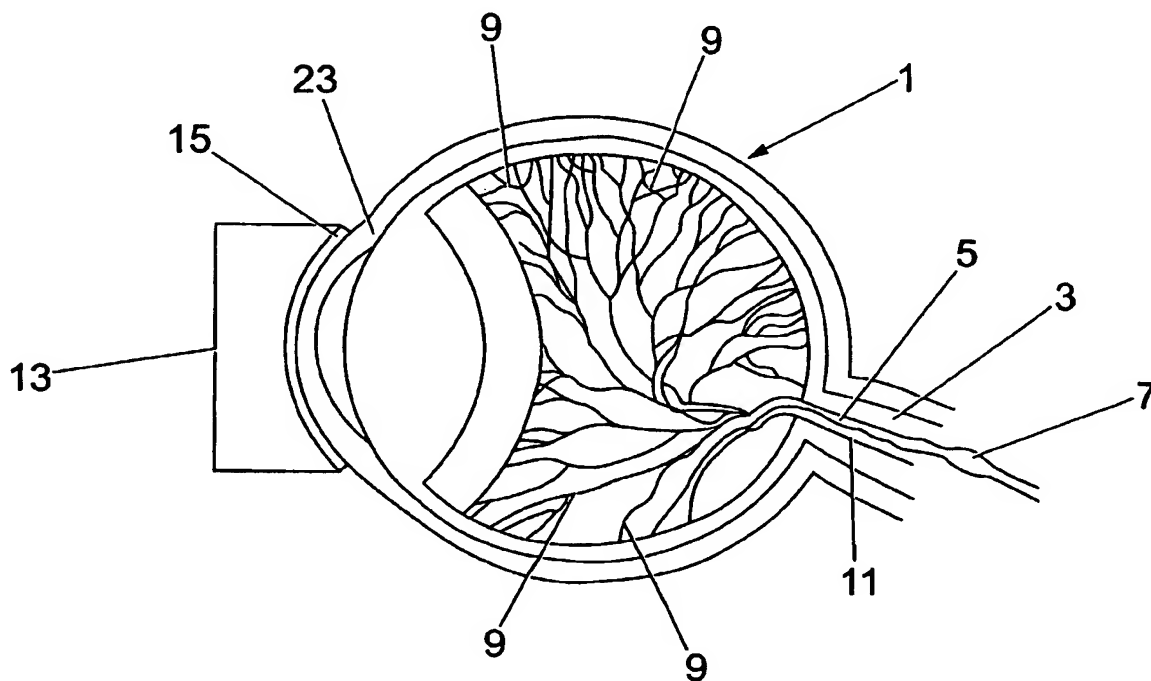
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(54) Title: **VASCULAR IMPEDANCE MEASUREMENT APPARATUS**



(57) Abstract: Apparatus and method for the measurement of vascular impedance of the ocular circulation *in vivo* are provided. A pressure pulse waveform is recorded from measurement of the intraocular pressure, and the velocity profile of blood flow in the retrobulbar circulation is recorded. These two readings are used to calculate the vascular impedance modulus.

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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 03/01729

**A. CLASSIFICATION OF SUBJECT MATTER**  
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Minimum documentation searched (classification system followed by classification symbols)  
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Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

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## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	POLSKA E ET AL: "RI in central retinal artery as assessed by CDI does not correspond to retinal vascular resistance." AMERICAN JOURNAL OF PHYSIOLOGY. HEART AND CIRCULATORY PHYSIOLOGY. UNITED STATES APR 2001, vol. 280, no. 4, April 2001 (2001-04), pages H1442-H1447, XP002254524 ISSN: 0363-6135	1-4, 6-11, 13-15, 18-20
Y	page H1442, left-hand column, line 8 - 16 page H1443, sections "Measurement of IOP" and "Measurement of center line red blood cell velocity using bidirectional LDV"  --- -/--	12,21

☒ Further documents are listed in the continuation of box C.

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>POWALOWSKI T ET AL: "NON-INVASIVE ULTRASONIC METHOD FOR THE BLOOD FLOW AND PRESSURE MEASUREMENTS TO EVALUATE THE HEMODYNAMIC PROPERTIES OF THE CEREBRO-VASCULAR SYSTEM" ARCHIVES OF ACOUSTICS, POLISH SCIENTIFIC PUBLISHERS, WARZAW, PL, vol. 10, no. 3, 1985, pages 303-314, XP000646828 ISSN: 0137-5075 section 1. "Introduction" -----</p>	12,21